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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,675	09/10/2003	Tim M. Townes	21085.0053U5	3735

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EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,675	TOWNES ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-19 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-19 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 2/09/2006 is acknowledged. Claims 1,2,4-19,21, 22 and 23 are pending in the instant application. Applicant amended claims 1,2,4-19 and 21, and canceled claims 3, 20, and 24.

Claims 1,2,4-19,21, 22 and 23 are currently under consideration.

The sections of title 35 U.S.C not included in this office action can be found in a previous office action. An action on the merits follows.

Oath/Declaration

The objection to the oath or declaration is withdrawn in view of applicant's submittal of a new oath and declaration.

Double Patenting

The rejection of claim 20 under the judicially created doctrine of double patenting over claims of U. S. Patent No. 5,877,288 is withdrawn in view of the cancellation of claim 20.

Claim Rejections - 35 USC § 102

The rejection of claim 20 under 35 U.S.C. 102(b) as being anticipated by Dong et al. {Dong et al. (February 1995) Arch. Biochem. And Biopys. 316:893-898}, is withdrawn due to the cancellation of claim 20.

The rejection of claim 20 under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,877,288 (3.2.1999) priority to (6.21.1993), is withdrawn due to the cancellation of claim 20.

The rejection of claim 20 under 35 U.S.C. 102(f) over US Patent No. 5,877,288 because the applicant did not invent the claimed subject matter, is withdrawn due to the cancellation of claim 20.

Claim Rejections - 35 USC § 112

The rejection of claims 1,2,4-19,21, 22 and 23 under 35 U.S.C. 112, first paragraph, is maintained, because the specification, while being enabling for "transgenic mouse whose genome comprises a human LCR γ-β hemoglobin switching DNA construct, wherein said genome is further homozygous for murine α- and β-globin knockout alleles such that said knockout alleles result in said mouse failing to synthesize murine hemoglobin, and wherein said hemoglobin switching construct is expressed such said mouse develops hemolytic anemia", does not reasonably provide enablement for a transgenic mouse comprising erythrocytes that produce a human hemoglobin without a switch locus, but fail to produce adult hemoglobin endogenous to said nonhuman mammal." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 2/09/2006 have been fully considered but they are not persuasive in overcoming the rejection the claims. Applicant argues that the declaration of Dr. Townes provides evidence that the switching construct is not required to produce the claimed mouse. Applicant argues that Dr. Townes states that the switch construct is needed to offset the

effect of transgenic sickle hemoglobin in the early developmental stages of the mouse, when reduced oxygen capacity is not tolerated like it is in an adult (Reply of 2/09/2006; pg. 6). It is noted that the claims are drawn to a mouse that comprises erythrocytes that produce human hemoglobin. The claims are not drawn to a specific developmental stage mouse, e.g. an adult mouse. Therefore the claimed mouse could express anti-sickling hemoglobin at one stage and sickling hemoglobin at another. In fact this is specifically what a mouse comprising the switch locus teaches, since it is well known in the art that fetal hemoglobin is inherently anti-sickling. Further, the remaining pending claims either specifically or broadly encompass a mouse comprising human sickling hemoglobin. Therefore the declaration of Dr. Townes actually provides direct support for the examiner's rejection based on scope of enablement because the argument indicates that the switch construct is required to make sickling mice. The implication is that the expression of sickling hemoglobin during fetal development is lethal. Applicant is reminded that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). Here the claims clearly encompass a mouse that expresses sickling hemoglobin in a fetal context. Neither the specification, nor the declaration of Dr. Townes provides any support for such mice. Therefore the rejection is maintained for reasons of record as stated above and in the office action of 10/11/05.

Claim Rejections - 35 USC § 103

The rejection of claims 1-19 under 35 U.S.C. 103(a) as being unpatentable over Paszty et al (Ref. A24) and Ciavatta et al (Ref. A9) taken with Rubin et al (Ref. A29) and Fabry et al (Ref. A12), is maintained.

Response to Arguments

Applicant's arguments filed 2/09/2006 have been fully considered but they are not persuasive. Applicant argues that there is no motivation for combining the teachings of the cited art and no reasonable expectation of success. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 19880; In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, the cited references describe the long-felt need for mouse models of human hemoglobin related diseases, such as thalassemia, and sickle cell anemia. Further, each of these references describe mouse models that were made in pursuit of filling this need. Finally, the Fabry et al. notes the problems related to the presence of endogenous mouse globins (Fabry et al. Abstract; pg. 419, Introduction) Therefore, the ordinary practitioner in the art would have had a clear motivation to make the claimed mouse.

In regards to the lack of reasonable expectation of success, applicant argues that the declaration of Dr. Townes indicates that high metabolic rate of the mouse requires efficient oxygen delivery and that the oxygen affinity of mouse and humans are significantly different. However, mice have higher blood levels of 2,3-diphosphoglycerate than do humans. Higher

levels of DPG change the binding affinity of hemoglobin to favor the metabolic environment of small mammals, such as mice. Therefore the ordinary practitioner in the art would have expected that the mouse would survive on human hemoglobin. Applicants further argue that the enablement arguments set forth by the examiner in the prior office action make the invention non-obvious. Applicant should note that the enablement arguments were in regards to the invention as previously broadly claimed. In fact, the invention as presently claimed would have been obvious to make since it could have been accomplished merely by breeding existing mouse lines and screening the offspring for the desired genotype. Therefore the rejection is maintained for reasons of record as stated above and in the office action of 10/11/05.

The rejection of claims 21-24 under 35 U.S.C. 103(a) as being unpatentable over Paszty et al and Ciavatta et al taken with Rubin et al and Fabry et al, as applied to claims 1-19 above, and further in view of Westphal (FASEB J, 1989), is maintained.

Response to Arguments

Applicant's arguments filed 2/09/2006 have been fully considered but they are not persuasive. It is noted that applicant did not specifically traverse this rejection. The rejection is maintained for reasons of record as set forth in the office action of 10/11/05.

No claims allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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